REMARKS/ARGUMENTS

Claims 1, 2, 4, 6-9, 11-18, 49-50, 60 and 61 are pending in the instant application. Claims 4 and 11-18 have been withdrawn. Applicants respectfully request rejoinder of these claims. Applicants have canceled claims 10, 51 and 52. Applicants reserve the right to pursue the subject matter of these claims in a continuation application. Applicants have amended claim 1. Support for the amendment to claim 1 can be found, for example, at paragraphs [0014] and [0054] of the instant specification. Applicants have also added new claim 61. Support for claim 61 can be found, for example, at paragraph [0037] of the instant specification. No new matter has been added.

Request for Reconsideration of Improper Finality of Rejection

Applicants submit that this Office Action has been improperly made final. Claims were newly rejected under 35 U.S.C. § 102 over Tabata *et al.* WO 03/13588 ("Tabata") and Caplan *et al.* U.S. Patent No. 5,486,359 ("Caplan"). These rejections under 35 U.S.C. § 102 over Tabata and Caplan involve newly cited art. A second Office action may not be properly made final when the examiner introduces a new ground of rejection that is neither necessitated by applicant's amendment of the claims, nor based on information submitted in an information disclosure statement filed during the period set forth in 37 C.F.R. § 1.97(c) with the fee set forth in 37 C.F.R. § 1.17(p).

Prior to the previous non-final Office action, claim 51 encompassed a pharmaceutical composition for the treatment of multi-organ failure, organ dysfunction or for wound healing comprising a therapeutic amount of mesenchymal stem cells. Thus, claim 51 as presently rejected is narrower in scope than claim 51 at the time of the mailing of the previous non-final Office action. Under the Examiner's rationale for anticipation (with which Applicants respectfully disagree) claim 51 should have been rejected in the previous non-final Office action. However, claim 51 was not rejected in the previous Office action under 35 U.S.C. § 102 over Tabata and Caplan. Moreover, no information disclosure statement was filed during the period set forth in 37 C.F.R. § 1.97(c) with the fee set forth in 37 C.F.R. § 1.17(p). Thus, this rejection introduces a new ground of rejection that is neither necessitated by applicant's amendment of the claims, nor based on information submitted in an information disclosure statement.

In light of MPEP 706.07(a), the rejections in the instant Office Action amount to rejecting a claim with art not previously cited when Applicants' amendment did not necessitate the rejection. Thus, Applicants submit that the finality of this rejection is improper.

Rejections under 35 U.S.C. § 102

The Examiner has maintained the rejection of claims 1, 2, 6-10, 49-50 and 60 under 35 U.S.C. § 102(a) for being anticipated by Imai *et al.* Ped. Nephrol. 17:790-794 (2002) ("Imai"). Applicants have canceled claim 10, rendering this rejection moot as it regards this claim. The Examiner argued that despite the claims being amended to encompass "isolated mesenchymal stem cells" that Imai still anticipates claims 1, 2, 6-10, 49-50 and 60. The Examiner alleged that the term "isolated" has not been accorded any particular definition in the specification.

Applicants respectfully disagree, but to facilitate prosecution, have amended claim 1, from which claims 2, 6-9, 49-50 and 60 depend. Claim 1 has been amended to be limited to mesenchymal stem cells that are expanded *in vitro* to produce an enriched population of mesenchymal stem cells and to a method of treating acute kidney dysfunction in a subject in need thereof. Imai does not teach this limitation. Further, claim 1 has been amended to be limited to the treatment of acute kidney dysfunction. Imai does not teach this limitation either.

As explained in the declaration under 37 C.F.R. § 1.132 by Robert Brenner, Imai does not teach the treatment of acute kidney dysfunction nor does it teach a subject in need thereof. Imai teaches an anti-Thy 1 antibody mediated glomerulonephritis (Thy 1 nephritis), a self-limiting disease to explore the involvement of bone marrow derived cells in glomerular remodeling.[1/] Thy 1 nephritis is a model of antibody-mediated glomerular disease.[2/] As the authors recognize, in Thy 1 nephritis normal mesangial cells (mesangial cells are macrophage like cells that are only found within the glomerulus) are disrupted (mesangiolysis), followed by an increase in the number of glomerular cells and subsequent glomerular remodeling.[3/]

Importantly, Thy 1 nephritis is not a model of classic acute kidney injury. Ischemia reperfusion injury is a completely different model of kidney injury. Renal artery clamping results in initial ischemia (an oxygen deprived state). Subsequent release of the renal artery clamp enables reperfusion of the ischemic kidney. Ischemia-reperfusion of this sort is a classic model

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1/ *See* Imai at page 792.
2/ *Id.* at left column.
3/ *Id.*

of renal tubular cell injury. It is the renal tubular cells that are the most susceptible to ischemic injury, as these cells normally live in a low oxygen environment. When the kidney is challenged by low oxygen tension, as is the case with renal artery clamping, it is the tubular cells that suffer the burden of injury. This is often referred to as acute tubular necrosis, or ATN. The initial tubular injury results in altered nephron architecture, obstruction, and reduced clearance. Importantly, ischemia reperfusion injury is not a form of primary glomerular cell injury, as is the case with the Thy 1 nephritis model. Similarly, the Thy 1 nephritis model does not directly involve the renal tubular cells, and this model is not characterized by obstruction and disturbed nephron architecture. Thus, Imai does not teach the treatment of acute kidney dysfunction nor does it teach a subject in need thereof.

Thus, Imai does not teach each and every limitation of claims 1, 2, 6-10, 49-50 and 60 and cannot anticipate them. Applicants respectfully request that this rejection be withdrawn.

The Examiner has rejected claims 51 and 52 under 35 U.S.C. § 102(a) for being anticipated by Tabata. Applicants have canceled claims 51 and 52, rendering this rejection moot.

The Examiner has also rejected claims 51 and 52 under 35 U.S.C. § 102(a) for being anticipated by Caplan. Applicants have canceled claims 51 and 52, rendering this rejection moot.

CONCLUSION

Applicant respectfully requests prompt examination in the application. If there are any questions regarding this Response, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Applicant believes no additional fees are due with the filing of this Response. However, if any additional fees are required or if any funds are due, the USPTO is authorized to charge or credit Deposit Account Number: **50-0311**, Customer Number: **30623**, Reference Number: **38447-201N01US**.

Respectfully submitted,

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